



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|-----------------|-------------|----------------------|---------------------|------------------|
| 09/281,474 | 03/30/1999 | MILIND RAJOPADHYE | DM-6958 | 7274 |

23914 7590 03/31/2004

STEPHEN B. DAVIS
BRISTOL-MYERS SQUIBB COMPANY
PATENT DEPARTMENT
P O BOX 4000
PRINCETON, NJ 08543-4000

EXAMINER

JONES, DAMERON LEVEST

| ART UNIT | PAPER NUMBER |
|----------|--------------|
|----------|--------------|

1616

DATE MAILED: 03/31/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Art Unit: 1616

ACKNOWLEDGMENTS

1. The Examiner acknowledges receipt of the amendment filed 12/22/03 wherein claim 1 was amended and claim 52 was added.

Note: Claims 1-10, 12-35, 48-50 and 52 are pending.

RESPONSE TO APPLICANT'S ARGUMENTS/AMENDMENT

2. The Applicant's arguments filed 12/22/03 to the rejection of claims 1-10, 12-35, and 48-50 made by the Examiner under 35 USC 103 and/or double patenting have been fully considered and deemed persuasive-in-part for the reasons set forth below.

Double Patenting Rejection

The provisional rejections of claims 1-10, 12-35, 48-50, and newly added 52 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over copending application numbers 09/465,300; 09/466,582; 09/599,364; 09/281,209; and 09/948,807 are MAINTAINED for reason of record in the office action mailed 7/2/02, Paper No. 22.

Note: It is duly noted that Applicant intends to rebut the double patenting rejections once all other rejections are withdrawn.

103 Rejection

The rejection of claims 1, 2, 12-15, 17, 19-23, 25, 27, 28, 31-35, 48, 49, and newly added claim 52 under 35 USC 103(a) is moot in view of the new rejection below.

Office Action Summary

Application No.

09/281,474

Applicant(s)

RAJOPADHYE ET AL.

Examiner

D. L. Jones

Art Unit

1616

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 22 December 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-10,12-35,48-50 and 52 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-10,12-35,48-50 and 52 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

NEW GROUNDS OF REJECTION

103 Rejection

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

4. Claims 1, 2, 12-15, 17, 19-23, 25, 27, 28, 31-35, 48, 49, and newly added claim 52 are rejected under 35 U.S.C. 103(a) as being unpatentable over Palladino et al (US Patent No. 5,780,426) in view of Sharma (US Patent No. 6,331,285).

Palladino et al disclose non-RGD cyclic peptides that inhibit the function of alpha(v)beta(3). Peptides pharmaceuticals and uses thereof are also disclosed. Therapeutic uses for the peptides include treating diseases such as cancer, osteoporosis, restenosis, and angiogenic-based disorders (see entire document, especially, abstract; columns 3-4, bridging paragraph). In addition, Palladino et al disclose that a detectable marker may be incorporated into the composition by a radiolabeled amino acid or attachment of a polypeptide or various methods of labeling which are known in the art. Labels for peptides include (1) labeling with a radioisotope (e.g., 125I or 131I), (2) metal binding domain, or (3) attaching labels by spacer arms of various lengths. The term 'label' as set forth in Palladino et al is directed to molecules that are either directly or indirectly involved in the production of a detectable signal of a complex. Thus, any label may be linked to or incorporated into the peptide structure

Art Unit: 1616

(column 6, lines 37-55; column 20, line 18 - column 21, lines 12). Diagnostic kits comprising the compositions may be generated as well (column 21, lines 23-55). While, Palladino et al does not disclose a specific species having all of the components (chelator, linker, and peptide) as set forth in Applicant's independent claims 1 and 52, the reference does suggest the presence of the components as set forth below.

Sharma discloses cyclic metallo-constructs that may be RGD receptor peptide mimics that comprise a metal ion binding backbone available for complexing with a metal ion and a biological function domain (columns 12-13, bridging paragraph; columns 13-14, bridging paragraph). The metal peptide backbone may be composed of side chains that make up a tetradentate peptide construct with N4, N3S, N2S2, NS3, N2SO or any combination thereof wherein nitrogen, sulfur, and oxygen atoms are utilized (column 27, lines 7-45; column 32, lines 26-44). Possible spacer sequences may be linked, directly, or indirectly to amino acids so as to form a continuous sequence (column 28, lines 23-35). Thus, for most applications, each peptide will include a metal ion complexing backbone which complexes a single metal ion. However, other applications may have a peptide backbone designed with a metal ion complexing backbone segment separated by one or more amino acid residues or other spacers or which the amino acid residues or spacers may, but do not have to, form a part of the functional group or biological function domain.

It would have been obvious to one of ordinary skill in the art to combine the teachings of Palladino et al in combination with those of Sharma and generate a compound and use thereof comprising a alpha(v)beta(3) targeting peptide-linker-

Art Unit: 1616

chelator combination because (1) Palladino et al disclose a composition comprising an alpha(v)beta(3) targeting moiety which may have a radioisotope present. As set forth by Palladino et al the targeting moiety may be labeled by any method known in the art. P labeling technique as disclosed in the reference is the incorporation of metal binding domains or the attachment of labels by spacer arms of various lengths (column 6, lines 37-55). (2) Sharma discloses that a spacer sequence may be incorporated into peptides. Specifically, any sequence which may be linked directly or indirectly to two amino acid residues so as to form a continuous sequence or one may have two discrete segments separated by one or more amino acid residues or other spacers. Hence, the skilled practitioner in the art would recognize that when Applicant's variables g, g', k, h', h", and "" are zero, the (W)h variable remains. Thus, when W is (aa)t wherein t is 1-10, you may have a single amino acid or an amino acid sequence present (attached to the targeting moiety). Thus, that amino acid or sequence is consistent with the moiety taught by Sharma which in itself may generate tetradentate peptide construct having N4, N3S, N2S2, NS3, N2SO or any combination thereof wherein nitrogen, sulfur, and oxygen atoms are utilized. Hence, the presence of a chelating moiety. It should be noted that based on the teachings of Sharma, the peptide may be directed or indirectly linked to the metal domain. Thus, the skilled practitioner would recognize that a linking group is optional to the chelating moiety.

Since both Palladino et al and Sharma encompass non-RGD cyclic peptide constructs, the references may be considered to be within the same field of endeavor. Thus, the references are combinable.

Art Unit: 1616

5. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP

§ 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

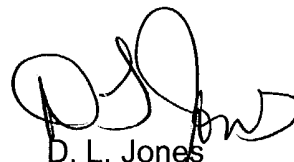
A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to D. L. Jones whose telephone number is (571) 272-0617. The examiner can normally be reached on Mon.-Fri., 6:45 a.m. - 3:15 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman Page can be reached on (571) 272-0602. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Art Unit: 1616

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



D. L. Jones
Primary Examiner
Art Unit 1616

March 29, 2003